

**REMARKS**

Claims 1, 3-15 and 17-21 are pending in the present application. Claims 11-15 and 19 have been withdrawn. Claim 1 is in independent form. Claims 1, 5, 7-10, 17 and 18 are amended. Claims 20 and 21 are newly-added. In view of the above amendments and following remarks, favorable reconsideration and allowance of the present application is respectfully requested.

Initially, Applicants appreciate the Examiner's indication that the references submitted in the Information Disclosure Statement filed on May 13, 2008 have been considered.

I. **CLAIM AMENDMENTS**

By the present Amendment, Applicants submit that claims 1, 5, 7-10, 17 and 18 are amended, and claims 20-21 are newly-added. Claims 5, 7-10, 17 and 18 are amended to clarify the subject matter that is already claimed and/or to place the claims in better form with U.S. practice (for example, by providing proper antecedent basis).

Support for amended independent claim 1 may be found, at least, in paragraph [0010] of the originally-filed Specification. Support for newly-added claims 20 and 21 may be found, at least, in paragraphs [0023] and [0027], respectively, of the originally-filed Specification.

Thus, Applicants submit that the claim amendments do not introduce new matter.

II. CITED ART GROUNDS OF REJECTION

(A) *Claims 1, 3, 4, 7, 8 and 17 stand rejected under 35 U.S.C. §103(a) as allegedly being unpatentable over Cheng et al. (hereinafter "Cheng"), U.S. Patent Publication No. 2002/0155586 in view of Frechet et al. (hereinafter "Frechet"), U.S. Publication No. 2004/0101442. Applicants respectfully traverse the rejection.*

i. INDEPENDENT CLAIM 1

Amended independent claim 1 is directed to a method for PCR amplification and detection of nucleotide sequences including (*inter alia*) "detecting hybridization events on the probe molecules immobilized at one of the analytical positions electrochemically with the aid of a microelectrode arrangement wherein detected nucleotide sequences alter impedance of the microelectrode arrangement." Applicants submit that the combination of Cheng and Frechet fails to explicitly teach, or otherwise suggest, the above features recited in amended independent claim 1.

a. THE COMBINATION OF CHENG AND FRECHET

As acknowledged by the Examiner on page 4 of the Action, Cheng teaches "[t]he capture probe-target hybrids are then detected using fluorophore-labeled reporter probes and the CCD-based optical imaging system employed for the portable instrument shown in FIG. 2." Cheng, paragraph [0092]. Thus, Cheng teaches that the hybrids are detected optically.

Applicants submit that the dimensions of optical measurement systems differ from the dimensions of electrochemical systems. Optical detection methods are spatially restricted to the wavelength of light with respect to the smallest detection limit. Electrochemical systems can be produced with much smaller detection electrodes and the concentrations of samples to be detected are also considerably smaller.

Cheng teaches that “[a]lternatively, a direct electrochemical voltammetric detection system may also be used...” Cheng, paragraph [0095] (emphasis added). Applicants submit that, in a voltammetric detection system, a current and a substance turnover is generated, which damages the layers on the electrodes. Thus, one of ordinary skill in the art would not be motivated use a direct electrochemical voltammetric detection system with the claimed method.

Furthermore, Cheng fails to teach, or suggest, that the detected marker sequences “alter impedance of the microelectrode arrangement” as recited in amended independent claim 1.

Applicants note that Frechet fails to teach, or suggest, an electrochemical measurement.

For at least these reasons, Applicants submit that Cheng in view of Frechet fails to explicitly teach, or otherwise suggest, a method for PCR amplification and detection of nucleotide sequences including “detecting hybridization events on the probe molecules immobilized at one of the analytical positions electrochemically with the aid of a microelectrode

arrangement wherein detected nucleotide sequences alter impedance of the microelectrode arrangement” as recited in amended independent claim 1.

Accordingly, Applicants respectfully request that the Examiner reconsider and withdraw the rejection to independent claim 1, and claims 3, 4, 7, 8 and 17 at least by virtue of their dependency on independent claim 1.

*(B) Claims 5 and 6 stand rejected under 35 U.S.C. §103(a) as allegedly being unpatentable over Cheng in view of Frechet and further in view of Ghodsian, U.S. Publication No. 2002/0115293. Applicants respectfully traverse the rejection.*

Ghodsian is directed to a chip device for sequencing long DNA fragments using optical detection. Ghodsian fails to teach, or suggest, electrochemical detection using a microelectrode arrangement wherein detected nucleotide sequences alter impedance of the microelectrode arrangement. Thus, Ghodsian fails to cure the deficiencies of Cheng and Frechet with respect to amended independent claim 1.

Applicants submit that claims 5 and 6, at least by virtue of their dependency on independent claim 1, are patentable over the combination of Cheng, Frechet and Ghodsian.

As such, Applicants respectfully request that the Examiner reconsider and withdraw the rejection to claims 5 and 6.

*(C) Claims 9, 10 and 18 stand rejected under 35 U.S.C. §103(a) as allegedly being unpatentable over Cheng in view of Frechet and further in view of Strizhkov et al. (hereinafter "Strizhkov"), Biotechniques (2000) 29:844-846, 848, 850-852, 854, 856-857. Applicants respectfully traverse the rejection.*

Strizhkov, directed to PCR amplification, teaches that "[t]he kinetics of amplification was measured in real time in parallel for all gel pads with a fluorescent microscope equipped with a charge-coupled device (CCD) camera." Strizhkov, Abstract. Thus, Strizhkov teaches using optical detection, not electrochemical detection using a microelectrode arrangement wherein detected nucleotide sequences alter impedance of the microelectrode arrangement. Thus, Strizhkov fails to cure the above-noted deficiencies of Cheng and Frechet with respect to amended independent claim 1.

Applicants submit that claims 9, 10 and 18, at least by virtue of their dependency on independent claim 1, are patentable over the combination of Cheng, Frechet and Strizhkov.

As such, Applicants respectfully request that the Examiner reconsider and withdraw the rejection to claims 9, 10 and 18.

III. PRIORITY GERMAN APPLICATION

Assuming that it would be helpful for the advancement of the present U.S. patent application, Applicants wish to point out that a patent (German Patent No. DE 102 69 819 B4) was granted for the priority German application.

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**CONCLUSION**

Accordingly, in view of the above, reconsideration of the rejections and allowance of each of claims 1, 3-15 and 17-21 in connection with the present application is earnestly solicited.

Should there be any matters that need to be resolved in the present application, the Examiner is respectfully requested to contact the undersigned at the telephone number below.

If necessary, the Commissioner is hereby authorized in this, concurrent, and future replies, to charge payment or credit any overpayment to Deposit Account No. 08-0750 for any additional fees required under 37 C.F.R. § 1.16 or under 37 C.F.R. § 1.17; particularly, extension of time fees.

Respectfully submitted,

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